159 Fundoplication for reflux induced cough in cystic fibrosis

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Reflux induced cough in patients with cystic fibrosis (CF) is a common but poorly recognised problem. Laparoscopic fundoplication may be a treatment for patients not responding to maximal medical therapy. Operative treatment may have the additional benefit of preventing non acid as well as acid reflux.
Patients with reflux cough were identified by the characteristic clinical history of extra-oesophageal reflux. Patients were offered fundoplication following failure of maximal medical therapy. All underwent oesophageal pH and manometry studies prior to surgery. Symptoms were assessed by the Leicester Cough Questionnaire (LCQ). Spirometry was performed pre- and postoperatively.
Four patients underwent fundoplication. The mean DeMeester score preoperatively was 45.5 (normal $\leqslant$14.8). Mean number of reflux episodes of 156 (normal $\leqslant$50). Longest episode lasted 54 minutes (mean 22.5 mins, normal 10 mins). Reported cough was highly associated with reflux episodes. Following surgery LCQ scores improved from a mean (range) of 68 (52–82) preop to 110 (100–124) afterwards. Spirometry increased from a mean of 0.86 to 0.93 (FEV1) and 2.17 to 2.36 (FVC). Reflux symptoms and quality of life were improved after fundoplication in this group of patients with proven acid reflux disease. Early spirometry improved a little but there was a trend to reduced exacerbation rate. Fundoplication appears safe even in this group of patients with marked spirometric impairment.
Recent studies indicate that surgery has an increasingly important role in treating reflux in patients requiring lung transplantation. Early fundoplication has been shown to reduce rates of bronchiolitis obliterans syndrome (BOS) and survival post transplant. We suggest agressive investigation and treatment for CF patients with the persistent dry cough characteristic of reflux.

160 Determinants of delivered dose from the I-neb® AAD® System

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The I-neb® AAD® System has been designed to deliver precise doses of drug to the patient. It is approved as a general purpose nebulizer in the EU and cleared for use with Ventavis® in the USA. The delivered volume is determined either by the volume of the metering chamber, or by the volume metered into the medication chamber. The metered volume (MV) and the drug concentration should therefore be important determinants of the delivered dose (DD). In order to test the hypothesis, we have analyzed the MVs and DDs of four drugs used in the treatment of patients with cystic fibrosis.
Three I-nebs for each drug tested were connected via a filter to a Harvard pump set to generate the CEN simulated breathing pattern. For tobramycin 1.5 mL was metered into the medication chamber, a metering chamber of delivery volume 0.3 mL was used for the three other drugs. The MV was assessed using a gravimetric method and was used to calculate the expected DD (the product of the MV and the drug concentration). The actual DD was assessed using a bioassay for colistimethate sodium, HPLC for tobramycin, and spectrophotometry for dornase alfa and salbutamol. Tests were performed in triplicate for each device/drug combination.
The calculated DD approximated the measured DD for each of the drugs, which proves the hypothesis that the MV and drug concentration are important determinants of the DD.
Precise doses of tobramycin, colistimethate sodium, dornase alfa and salbutamol sulphate can be delivered into simulated breathing by the I-neb AAD System.

Drug	MV* (SD)	Drug concentration	Calculated DD	Measured DD (SD)
Tobramycin	1456 mL (49 mL)	60 mg/1 mL	87.36 mg	75.9 mg (6.6 mg)
Colistimethate sodium	311.2 mL (18.0 mL)	1 MIU/1 mL	311.2 kIU	324.9 kIU (15.8 kIU)
Dornase alfa	318.3 mL (5.3 mL)	1,000 U/1 mL	318.3 U	296.7 U (13.9 U)
Salbutamol sulphate	317.2 mL (6.0 mL)	2.0 mg/1 mL	634.4 mg	605.1 mg (10.1 mg)

* minus 0.1 mL residual volume in the medication chamber for tobramycin.

161 PortaNeb® or CR60®? Inhalation of tobramycin (TOBI®) with the Pari LC Plus® nebuliser: an *in vivo* pilot study

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Aim: The CR60® compressor produces small particles and is said to shorten nebulisation time. Two compressors (CR60® and PortaNeb® (PN)) for inhalation of tobramycin (Tobi®) were compared, using the Pari LC Plus® (PLP) nebuliser, in a pilot study. The pharmacokinetics (PK; safety (Cmax)), pulmonary deposition (AUC_{0-6}), nebulisation time, bronchoconstriction and patient's experience were compared.
Methods: Ten CF patients participated in an open, randomised cross-over study with 300 mg tobramycin using both compressors. FEV1 and FVC were registered before and after inhalation. Tobramycin lung deposition was indirectly determined by measuring tobramycin serum concentrations and PK analysis. The patient's experience was documented using a questionnaire. The Wilcoxon signed ranks test was used for statistical analysis. Results are presented as median and range.
Results: PK: C_{max}: CR60 0.70 (0.53–2.49) vs PN 0.54 (0.41–1.95) mg/L, $p = 0.005$) and AUC_{0-6}: (CR60 2.54 (1.98–6.65) vs PN 2.01 (1.55–6.18) h.mg/L, $p = 0.017$) were different. T_{max} CR60 was earlier (0.64 (0.59–0.72) vs 0.85 (0.78–1.13) h, $p = 0.005$). Lung function tests indicated bronchoconstriction in 3 patients (2xPN;1xCR60) versus subjective experienced chest tightness in 7 patients (CR60® > PN).
No differences were observed regarding ease of administration and noise. A shorter nebulisation time of 13.2 (11.1–15.8) min was observed (CR60®), compared to PN 16.1 (11.8–19.4) min ($p = 0.022$), which was the main reason why patients preferred the CR60® ($n = 7$).
Conclusion: Inhalation of tobramycin (TOBI®) is safe using the PLP nebuliser and PN or CR60® compressor. The latter may be advantageous due to a shorter nebulisation time and larger pulmonary deposition. The patient's preference is of critical importance.

162 Characteristics of the patients with cystic fibrosis

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Objective: To demonstrate the clinical and laboratory characteristics of the patients with cystic fibrosis.
Material and Methods: The data files of 49 patients with cystic fibrosis followed by Department of Pediatrics in Dokuz Eylul University were evaluated retrospectively.
Results: Sixteen (32.7%) of 49 patients were girls, 33 (67.3%) were boys. The ages of patients varied between 8–239 months (85.9±53.3) and the ages at the diagnosis varied between 1.5 and 168 months (31.2±41.4). Consanguity was found in 13 (26.6%) of the patients' parents. Two of the patients had siblings with cystic fibrosis. All of them except one had findings of pulmonary involvement, 29 (59.2%) exocrine pancreas insufficiency, 22 (44.9%) malnutrition, 21 (42.9%) recurrent diarrhea, nine (18.4%) pseudobartter syndrome and one (2%) meconium ileus in the newborn period. Three (6.1%) patients died because of respiratory failure. The sweat tests varied between 68–172 mEq/L (101.7±22.6). The mutation rate that was detected in our patients is 35.2%. *Pseudomonas aeruginosa* colonisation was found in six (12.2%) patients and multiresistant *Pseudomonas aeruginosa* in two (4.1%) of them. Fifteen (30.6%) patients recieved inhaled steroid, 21 (42.9%) bronchodilatator, five (10.2%) aerosolized antibiotic therapy and five (10.2%) recombinant human deoxyribonuclease therapy.